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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,119	03/11/2004	Yih-Lin Chung	55701-004002	8809

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EXAMINER	
HUGHES, ALICIA R	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

INFO@ORTPATENT.COM

Office Action Summary	Application No.	Applicant(s)	
	10/798,119	CHUNG, YIH-LIN	
	Examiner	Art Unit	
	ALICIA R. HUGHES	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *2-4,6-10,12,13 and 18-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1, 5, 11, and 14-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims and Examination

Claims 1-21 are pending. However, only claims 1, 5, 11, and 14-17 are the subject of this Office Action, as claims 2-4, 6-10, 12, 13, and 18-21 are withdrawn from consideration, being drawn to a non-elected invention. See 37 C.F.R. 1.142(b).

Applicant's arguments and amendments filed on 17 December 2007 in response to the Final Rejection filed by this Office on 01 October 2007 have been fully considered, but they are not deemed to be persuasive. Rejections and objections not reiterated from previous office actions are hereby withdrawn.

The finality of this Office's Action of 01 October 2007 is hereby withdrawn so that new rejections may be applied and taken together with the following reiterations and clarifications, they constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 U.S.C. §112.1

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5, 11, and 14-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains,

or with which it is most nearly connected, to make and/or use the invention. Specifically, there is a lack of support in the disclosure for the treatment of all cancerous tumors.

Support for Rejection

In regards to the present rejection, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include:

1) Nature of invention;

2) State of the art;

3) Level of ordinary skill in the art;

4) Level of predictability in the art;

5) Amount of direction and guidance provided by the inventor;

6) Existence of working examples;

7) Breadth of claims; and

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The relevant factors are addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

Applicant has argued that the Office mistakenly construes claim 1 to apply to cancer treatment when in essence, the claim is not so directed to cancer but rather to side effects associated with therapeutic gain. This argument is not persuasive in that the claim is directed to "increasing therapeutic gain in chemotherapy or radiotherapy for malignant ... disease"

(emphasis added). When assigning claims their broadest reasonable interpretation, malignant may be defined as cancerous.

While the state of the art is relatively high with regard to the treatment of specific cancers, the state of the art with regard to treating cancer broadly is underdeveloped. In particular, there is no known anti-cancer agent or combinations thereof, that is effective against all cancerous tumor types. The Cecil reference (cited by Examiner on the attached form PTO-892), clearly shows that for the various known cancerous tumor types, there is not one specific chemotherapeutic agent or agents that is effective for each and every type of cancer or tumor, which is the subject matter encompassed by the present claims, (see Cecil at page Table 198-5 at page 1065; Tables 198-6 and 198-7 at page 1066; Table 198-8 at page 10684 and Table 198-9 at page 1071).

3) Level of ordinary skill in the art.

The level of ordinary skill in the art is high and would include the skill possessed by a person holding a degree such as a doctor of medicine degree. However, given the state of the art as set forth above, the artisan is currently unaware of any one particular anti-cancer agent, or combinations thereof, that is effective in treating all known types of cancer.

4) Level of predictability in the art.

The lack of significant guidance from the present specification or prior art with regard to the treatment of all cancers or tumors in a patient with any known anti-cancer or anti-tumor formulation imparts a significant degree of unpredictability in practicing the invention as presently claimed.

5) Amount of direction and guidance provided by the inventor.

The guidance given by the specification is to generally administer the claimed active agent(s) to treat cancers or tumors broadly.

6) Existence of working examples.

None of the examples in the present specification address the treatment of any particular cancer type, much less cancers in general.

7) Breadth of claims.

The complex nature of the subject matter to which the present claims are directed is exacerbated by the breadth of the claim. The claims are extremely broad due to the vast number of possible cancer/tumor types represented by the term "cancer."

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The specification does not enable any person skilled in the art to which it pertains to make or use the invention commensurate in scope with this claim. Applicants have failed to provide guidance and information to allow the skilled artisan to ascertain that the present active agent is effective against all types of cancerous tumor types.

Further Burden on the Examiner for Making a Rejection Under 35 U.S.C. § 112 First Paragraph

As set forth in *In re Marzocchi*, 169 USPQ 367, 370 (CCPA 1971):

> [A] [s]pecification disclosure which contains teaching of manner and process of making and using the invention in terms corresponding to the scope to those used in describing and defining subject matter sought to be patented must be taken as in compliance with enabling requirement of first paragraph of 35 U.S.C. 112 *unless there is reason to doubt the objective truth of statements contain therein which must be relied on for enabling support*; assuming that sufficient reason for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis, such a rejection can be overcome by suitable proofs indicating that teaching contained in specification is truly enabling. (emphasis

added).

Here, the objective truth of the statement that cancer, of a non-restricted nature, could be successfully treated is doubted because the art (see the references relied upon *infra*) teaches that, at best, that only certain neoplastic diseases may be treated with only certain compounds or combinations thereof. Given this, the treatment of all known cancers is merely a possibility and not a treatment outcome that could be accomplished with a reasonable degree of certainty or without a burden of undue experimentation, i.e., determining for which such diseases the claimed formulation could treat.

Summary

As the cited art and discussion above establish, practicing the claimed method in the manner disclosed by Applicants would not imbue the skilled artisan with a reasonable expectation that cancers of all types could be effectively treated with the presently claimed formulations. In order to actually achieve the claimed objective, if at all possible, it is clear from the discussion above that the skilled artisan could not rely on Applicants' disclosure as required by 35 U.S.C. § 112, first paragraph in light of the state of the art. Given that the art fails to recognize and Applicant has failed to demonstrate that all known cancers/tumors could actually be treated, the skilled artisan would be faced with the impermissible burden of undue experimentation in order to practice this embodiment of the claimed invention.

Claims 1, 5, 11, and 14-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains,

or with which it is most nearly connected, to make and/or use the invention. Specifically, there is a lack of support in the disclosure for increasing therapeutic gain in chemotherapy and radiotherapy for ***all*** proliferating malignant and non-malignant diseases. There is no known panacea and while the disclosure does provide support for the promoting radiation-induced wound healing in mucositis and dermatitis, support is not found for all malignant and non-malignant diseases.

Claims 1, 5, 11, and 14-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

No mechanism of action or data is provided to support Applicant's claim for "preventing complications or sequelae of a disorder, both of which are induced by radiation or chemotherapy." While indeed one may reduce complications, there is no evidence to substantiate a claim that complications may be eliminated altogether.

Claim Rejections – 35 U.S.C. §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 5, 11, and 14-16 are rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 5,877,213 [hereinafter referred to as "Samid"].[1]

[1] Cited on PTO Form 892 filed on 23 March 2007.

This Office's arguments from its actions of 23 March 2007 and 01 October 2007 are incorporated herein by reference in their entirety.

The Applicant's argument that Samid does not establish a *prima facie* case of obviousness, because the present invention is distinguishable due to its focus on promoting cell proliferation and survival rather than promoting cell death has been considered, but it is not deemed persuasive for the reasons of record set forth in this Office's previous actions mentioned *supra*. Additionally, Applicant now argues that Samid is an inapplicable reference, because of the patient population the hyperacetylating agent is to treat. Applicants argue that Samid treats patients with anemia, cancer, AIDs or severe β-chain hemoglobinopathies rather than those patients suffering from chemotherapy or radiotherapy induced side effects and therefore, is not applicable as prior art in the instant case.

As noted previously, claims are to be given their broadest reasonable interpretation and the claims as written in this application, apply for increasing therapeutic gain for either proliferating malignant or nonmalignant diseases wherein a patient undergoes radiotherapy or chemotherapy and anemia, cancer, AIDs or severe β-chain hemoglobinopathies are all either malignant or nonmalignant diseases.

In light of the foregoing, it would have been *prima facie* obvious to one of ordinary skill in the art to administer sodium phenylbutyrate in the manner prescribed by Samid, in combination with radiotherapy, as a method of treating various maliginancies and non-malignant diseases.

Claims 1 and 17 are rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 5,877,213 [hereinafter referred to as "Samid"] in view of Shufeng, Z., et al., *5,6-Dimethylxanthenone-4-acetic acid (DMXAA): A New Biological Response Modifier for Cancer Therapy*, Investigational New Drugs, vol. 20, 2002, pages 281-295 [hereinafter referred to as "Shufeng, et al."].[2]

The teachings of Samid, taught in this Office's actions of 23 March 2007 and 01 October 2007 are incorporated herein by reference as are the teachings of Shufeng et al from this Office's action of 01 October 2007 as well as the arguments, supra, regarding the applicability of the Samid reference to the instant set of claims.

One of ordinary skill in the art would be motivated to combine the teachings of Samid with the teachings of Shufeng et al., because the references teach overlapping subject matter, most notably, the treatment of cancer with anti-cancer/anti-tumor agents.

In light of the foregoing, one of ordinary skill in the art would be motivated to apply the teachings of Samid and the teachings of Shufeng et al to the present invention, because DMXAA is an anti-cancer agent/biological response modifier that when combined with radiotherapy and/or phenylacetic acid and its pharmaceutically acceptable salts and derivatives, including sodium phenylbutyrate, effectively treats various cancers. When used together, in light of the foregoing, it would have been *prima facie* obvious to one of ordinary skill in the art that the proliferation of cancers and their associated tumors would be treatable through the combination therapy of sodium phenylbutyrate and DMXAA with radiotherapy.

[2] Cited on PTO Form 892 filed on 23 March 2007.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alicia Hughes whose telephone number is 571-272-6026. The examiner can normally be reached from 9:00 AM to 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached at 571-272-0718. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR of Public PAIR. Status information for unpublished applications is available through Public PAIR only. For information about the PAIR system, see http://pair-direct-uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Alicia R. Hughes/

Examiner, Art Unit 1614

/Raymond J Henley III/

Primary Examiner, Art Unit 1614